of astral microtubules with the bud neck. Most remarkably, maintaining such attachments beyond anaphase onset prevented these spindles from elongating properly between mother and bud and frequently led to their elongation in the mother cell (Figure 1B). Thus, ubiquitination negatively controlled the behavior of the Kar9-decorated microtubules and their interaction with the cortex at the cleavage plane. Furthermore, this regulation was especially important after the metaphase–anaphase transition to maintain the proper position of the spindle relative to the cleavage plane. The authors propose that ubiquitin serves as a signal to dissociate Kar9 from Myo2 and reduce interactions between astral microtubules and the bud neck. But what is the exact function of this regulation?

It may be that microtubules continuously cycle between attachment and ubiquitin-dependent detachment from the bud neck. As the authors propose, this cycling could have the function of actually positioning the spindle close to the neck, explaining the spindle positioning defect observed when ubiquitination is impaired. However, in wild-type cells attachment to the bud neck is prominent during most of metaphase and starts to be resolved only as the cells approach anaphase onset. Thus, this and the phenotype observed in these cells suggest that dissociation of microtubules from the cleavage apparatus is in fact a necessary transition step from early spindle positioning to allowing spindle elongation. Therefore, the data reported by Kammerer *et al.* [9] demonstrate for the first time that whereas microtubule attachment to the cleavage apparatus plays a central role in spindle positioning during metaphase, at anaphase onset detachment becomes essential for the maintenance of spindle positioning with respect to the cleavage apparatus.

This brings us back to the mechanisms controlling cleavage furrow positioning in higher eukaryotes. As discussed previously, like fungi, interactions between astral microtubules and the cleavage apparatus occur in higher eukaryotes and are important for the positioning of the cleavage furrow relative to the spindle. Perhaps, the apparent paradoxes described over the years also reflect the necessity of two independent mechanisms involving different modes of interaction between microtubules and the cleavage apparatus as the cells progress from metaphase into anaphase. In other words, higher eukaryotes must perhaps also transit from a stage in which the spindle asters interact with the middle of the cell to a later stage when these interactions need to be released to allow spindle elongation (Figure 1A). This could at the same time be the point when the spindle midzone becomes more important than the spindle asters. The study by Kammerer *et al.* [9] elucidates a mechanism that may have implications for the spatial coordination of the cleavage apparatus and the spindle in higher eukaryotes as well. Therefore, we suggest that ubiquitination might also regulate interactions between microtubules and the cleavage apparatus in higher eukaryotes.

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Touch Perception: How We Know Where We Are Touched

The brain localizes touch not only on the skin, but also in three-dimensional space. A new study links behavioral findings in humans with neurophysiological findings in monkeys and suggests a model of how recoding from skin to space may be accomplished.

Tobias Heed

The sensory homunculus, located along the postcentral gyrus, may be the most widely known brain region. It maps sensation from the skin onto an orderly array of brain regions which roughly resemble the order of our body parts. When asked how the brain can know where our body was touched, we might therefore be quick to think that all that is needed is to identify which neurons in the homunculus were activated by the touch. Yet, because we can move our bodies so flexibly, the location of a touch is not only defined by where it was felt on the skin: a touch to, say, the hand may be located anywhere between the head and the toes, depending on our body posture at the moment of touch. To know this spatial location is important to make a motor response towards the touch, for example to swat away an insect that might be about to sting. It is also important to integrate tactile information with information from the other senses, most importantly vision.

Remapping of touch perception has thus often been investigated in multisensory contexts. Single cell recordings in monkeys have revealed that neurons in the ventral intraparietal

area (VIP) of the intraparietal sulcus (IPS), as well as in the premotor cortex of monkeys feature a tactile receptive field on the skin, and a visual receptive field for the space around the tactile receptive field. The neuron always responds to the space near the tactile receptive field, independent of where the body part is located, and of which part of the retina is currently seeing it [1,2]. To achieve this tactile–visual alignment, the brain must constantly match body posture with visual information. In humans, visual stimuli are specially processed when they occur near the body [3,4], suggesting that similar remapping mechanisms are at work in the human brain. For example, some patients overlook a visual stimulus near their hand when the other hand receives a touch at the same time, but they can detect the visual stimulus is in the same spatial location as before, but the hand is held somewhere else [5]. In fact, when tactile processing was disrupted in humans by applying repetitive transcranial magnetic stimulation (rTMS) to the human homologue [6] of monkey VIP, a touch to the right hand enhanced perception of visual stimuli in right space, even when the hand was crossed over to the left space, indicating that touch remapping was disrupted [7].

In a study reported in this issue of *Current Biology*, Azanon *et al.* [8] applied single pulse TMS to the same brain structure, VIP, while participants made judgments about the relative elevation of two touches, one to the arm and one to the face. Arm posture varied from trial to trial, and so did the location of the two stimuli. This task depends on knowing where the two stimuli are in space. They must therefore be remapped into external spatial coordinates. Compared to TMS stimulation to a control site, TMS over VIP resulted in a decrease of localization precision, implying that VIP is involved in the remapping of touch also in a purely tactile task.

A number of behavioral and electrophysiological studies in humans had previously suggested that touch is remapped not only when the context calls for it (as in crossmodal integration). Recoding from skin to space rather seems to be a default process, providing the brain with external spatial coordinates for any touch we perceive [9-13]. This automatic recoding is nevertheless tightly related to vision: congenitally blind individuals, who do not develop a visual system, do not automatically remap touch stimuli into external space; in contrast, people who lost their sight later in life do remap touch information, even after extensive periods of blindness [14,15]. That TMS over the same brain site disrupted crossmodal visual-tactile [7] and purely tactile [8] processing confirms that VIP is involved not only in merging touch with vision, but more generally in representing touch in an external-spatial, vision-related coordinate system.

The study by Azanon *et al.* [7] also advances our understanding of the role played by VIP in the remapping process. The authors devised two important control studies. In the first, they showed that judgments of arm posture were not affected by TMS over VIP. Thus, the role of VIP is not merely the representation of the body's current posture. In the second control study, judgments of two stimuli on the same arm were equally unaffected by TMS over VIP. Because arm posture does not affect the relative location of the two stimuli on the arm, their distance can be judged independent of any remapping. This control therefore implies that localization of touch on the skin was not impaired. The role of VIP must therefore be directly related to the remapping of touch per se, i.e. the integration of skin location and body posture to localize a tactile event in space.

From these results, Azanon *et al.* [7] sketch a model of tactile remapping, posing that skin-based localization of touch is mediated by primary (SI) and secondary (SII) somatosensory cortex. Posture, in turn, is computed by area 5 in the anterior part of the parietal lobe. VIP, they suggest, integrates touch and posture and provides external spatial coordinates of touch as output to other regions. This model constitutes a good starting point to understand the spatial processing of touch in the brain and could be extended to accommodate findings from related research. For one, VIP is part of a larger network involving also part of the premotor cortex [16], and it will be important to differentiate more clearly the different roles of these two areas in touch remapping. Furthermore, although SII is thought to be crudely organized in a body map-like fashion, its processing is modulated by posture in monkeys [17]. Similarly, in humans event-related potentials in response to touch, thought to originate from SII, systematically vary with changes in body posture [11]. Interestingly, VIP projects to SII [18]; postural influences may therefore be relayed to SII after having been remapped in VIP. Finally, visual information about body posture is presumably relayed from posterior areas and integrated with proprioceptive information about posture along the intraparietal sulcus [19], probably contributing to the remapping of touch in VIP as well.

In short, the new work of Azanon *et al.* [7] suggests that touch is remapped into external spatial coordinates by parietal area VIP, linking neurophysiological work in monkeys with behavioral findings in humans. Remapping is shown to be a process distinct from posture representation and localization on the skin. It will be exciting to discover the role of the other brain regions involved in the remapping process.

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Cell Migration: MIM Takes the Driver's Seat

A recent study reports a novel and conserved function for the I-BAR protein MIM in guiding cell migration: MIM has an anti-endocytic activity that moderates intracellular signalling of guidance cues by sequestration of cortactin.

Véronique Van De Bor and Stéphane Noselli*

Guided cell migration is essential during embryonic development for tissue morphogenesis, as well as in the adult for wound healing and the immune response [1–3]. Directed migration requires accurate reading of external guidance signals, but it is not yet clear how cells can sense variations in surrounding guidance cues and rearrange their cytoskeleton to adjust the direction in which they are migrating. It has been proposed that cell steering depends on polarized endocytosis of guidance receptors leading to the formation of a front and a rear in migrating cells [4,5]. One of the main challenges in the field is to identify regulators of endocytosis that are responsible for such spatial restriction of intracellular signalling. In a recent study published in the *Journal of Cell Biology*, Quinones *et al.* [6] demonstrated that the inverse Bin/Amphiphysin/Rvs (I-BAR) protein missing-in-metastasis (MIM) orchestrates directional migration through an anti-endocytic function. This study provides the first mechanistic link between a member of the I-BAR protein family and directed cell migration.

The BAR protein family is involved in endocytosis and vesicle trafficking in all eukaryotes. BAR proteins carry a crescent-shaped BAR domain, which is involved in membrane bending and curvature stabilisation through specific lipid interactions. Binding of BAR proteins to membranes triggers the assembly of protein complexes that promote actin cytoskeleton assembly near vesicles, thus positively regulating endocytosis [7]. MIM belongs to a new subgroup of the BAR family, characterised by the presence of an IRSp53-MIM homology domain (IMD) or inverse BAR (I-BAR) domain, which displays an inverted, convex shape. This reversal of the conformation of the BAR domain in I-BAR proteins is thought to provide an antagonistic activity towards BAR proteins during endocytosis [8–11]. To elucidate the role of MIM, Quinones *et al.* [6] combined analysis of fibroblasts in culture with analysis of the migration of border cells in *Drosophila* ovaries. Border cells undergo directional migration through two guidance receptor tyrosine kinases, the *Drosophila* EGF receptor (DER) and the PDGF/VEGF-like receptor (PVR) [12–17]. The authors first demonstrated, using lipid vesicle co-sedimentation assays, that vertebrate MIM and its *Drosophila* orthologue dMIM have conserved lipid-binding properties. They next quantified the rate of transferrin or EGF internalisation and recycling in cultured fibroblasts, as well as lipophilic dye uptake in live border cells. These experiments showed that alteration of MIM function increases endocytosis and the duration of EGF signalling. Remarkably, live-imaging experiments revealed that the absence of MIM is associated with impaired directional migration in response to guidance cues. These findings suggest that MIM regulates guided cell migration through its ability to inhibit receptor-mediated endocytosis and therefore controls the capacity of cells to sense directional migratory cues.

To unravel the mechanism by which MIM steers migrating cells, Quinones *et al.* [6] combined biochemical and genetic approaches. Using pull-down and co-immunoprecipitation assays they found that MIM directly binds cortactin, a conserved cortical actin-binding protein that promotes polymerisation and rearrangement of the actin cytoskeleton at the membrane for the formation of lamellipodia, invadopodia and endocytic vesicles [18,19]. Cortactin is a major substrate of the Src tyrosine kinase and previous studies showed that mutation of either *src* or *cortactin* leads to defects in border cell migration; however, it was not clear how Src or cortactin regulate directional movement [20]. Interestingly, cortactin is also part of the pro-endocytic complex assembled by the BAR family protein endophilin and its binding partner CD2AP [19]. Quinones *et al.* [6] provide genetic evidence that the pro-endocytic CD2AP–endophilin complex acts antagonistically to MIM, both in fibroblasts and in border cells. Indeed, upon EGF stimulation of fibroblasts, MIM competes with CD2AP–endophilin for cortactin binding, as revealed by the kinetics of cortactin association with vertebrate MIM or the